

Attorney Docket No. P63187US2
Application No. 10/722,467

Remarks/Arguments:

Applicants wish to thank the examiner for providing the initialed Form PTO 1449, attached the instant Office Action, as previously requested.

Claims 12-20, previously presented, are pending.

Claims 1-11 are canceled, without prejudice or disclaimer.

Claims 12-20 stand rejected under 35 USC 103(a) as being allegedly unpatentable over US 4473560 (Biere or Biere et al.) in view of US 5488041 (Barbier or Barbier et al.) and further in view of The American Journal of Medicine, 101, 1996, 339-340 (Siris). Reconsideration is requested.

An obviousness, i.e., §103(a), analysis requires determining every difference between the claims and the cited prior art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 230 USPQ 416 (Fed. Cir. 1986). To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 180 USPQ 580 (CCPA 1974). A "ground of rejection is simply inadequate on its face . . . [when] the cited references do not support each limitation of [the] claim." *In re Thrift*, 63 USPQ2d 2002, 2008 (Fed. Cir. 2002).

In the context of a rejection for obviousness under §103, the "Examiner bears [both] the initial burden . . . of presenting a *prima facie* case of unpatentability" and "the ultimate burden of persuasion on the issue." *In re Oetiker*, 24 USPQ 1443, 1444 and 1447 (Fed. Cir. 1992).

The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art *would lead* that individual to combine the relevant references. . . . Indeed, the teachings of the references can be combined only if there is some suggestion or incentive to do so.

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Ex parte Obukowicz, 27 USPQ2d 1063, 1065 (BPA&I 1992) (*emphasis, added*).

In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*,^[1] preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, that one having ordinary skill in the art *would have been led* to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention [*citations, omitted*].

Ex parte Levengood, 28 USPQ2d 1300, 1300-01 (BPA&I 1993)(*emphasis in original*).

One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988).

It is impermissible within the framework of §103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.

In re Hedges, 228 USPQ 685, 687 (Fed. Cir. 1986).

The fact that all elements of a claimed invention are known does not, by itself, make the combination obvious. *Ex parte Clapp*, 227 USPQ 972 (BPA&I 1985). Merely because the PTO can find two isolated disclosures that can theoretically be combined in such a way as to meet the application claims does not render the combination obvious "unless the art also contains something to suggest the desirability of the proposed combination." *In re Bergel*, 130 USPQ 206, 208 (CCPA 1961).

The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.

In re Fritch, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992).

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When prior art references require selective combination . . . to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself. . . There must be "something in the prior art to suggest the desirability, and thus the obviousness, of making the combination" [citation omitted].

Interconnect Planning Corp. v. Feil, 227 USPQ 543, 551 (Fed. Cir. 1985).

The rejected claims are specifically directed to a new, therapeutic use for a limited number of known bisphosphonic acid derivatives. That is, the present/rejected claims provide a method of "treating lameness caused by osteoarthritis" [osteoarthritis being synonymous with osteoarthritis, both words are used, interchangeably, in the following remarks], which treatment involves administering an effective amount of a (known) bisphosphonic acid derivative to a subject—human or animal—not suffering from fractures, wherein the bisphosphonic acid derivative is selected from:

- 1-hydroxyethylidenebisphosphonic acid and its sodium salts;
- 2-pyrid-2-ylethylidenebisphosphonic acid and its sodium salts;
- phenoxymethylenebisphosphonic acid and its salts;
- thiomorpholinomethylenebisphosphonic acid and its salts;
- 4-chlorophenylthiomethylenebisphosphonic acid and its salts;
- 1-hydroxy-2-(3-pyridyl)ethylidenebisphosphonic acid and its sodium salts;
- 1-hydroxy-2-(2-imidazolyl)ethyl-1,1-bisphosphonic acid and its salts; and
- 2-hydroxyethylidene-2-(3-pyridyl)-1,1-bisphosphonic acid and its sodium salts.

The statement of rejection alleges that Biere fully meets present claim 12, except for the recited "bisphosphonic acid derivative" and accept for "directly the treatment of lameness caused by osteoarthritis" (Office Action, page 4). The "bisphosphonic acid derivative" (other rejected claims) is allegedly met by Barbier, which teaches using the bisphosphonic acid derivative in a method of promoting bone repair, which method "is particular suitable following a fracture or bone surgery"

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(Office Action, page 4) [referring to Barbier, column 3, lines 10-35]. Further still, the rejection alleges that Siris meets the limitation "treating lameness caused by osteoarthritis" on the rejected claims, as well as using the "bisphosphonic acid derivative," recited in the rejected claims, in the allegedly disclosed method.

Thus, according to the statement of rejection (Office Action, page 7), allegedly:

It would have been obvious to one of ordinary skill in the art . . . to use the compounds of Barbier et al. [recited in the present claims] in the treatment of lameness caused by osteoarthritis (in horses) as Biere et al. teaches that the antiarthritic [*sic*, antiarthritic] activity of the bisphosphonic acid derivatives is useful for the therapy of . . . osteoarthritis . . . and other related diseases of the collagen and the skeletal system (osteoporosis and Paget's disease), further Barbier et al. disclose the currently claimed compositions as suitable for vet[er]inary use (thus encompassing horses) and Siris teaches that Paget's disease can induce osteoarthritis, causes localized bone pain (which is one source of lameness) and is treatable with the currently claimed compounds.

The statement of rejection also relies on the decision *Atlas Powder Co. v. Rieco Inc.*, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999), cited in MPEP 2112.01, as holding the "discovery of a previously presented unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning does not render the old composition patentability new to the discoverer" (emphasis added). "Thus" the statement of rejection alleges (Office Action, page 7)," the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable," citing in support *In re Best*, 195 USPQ 430, 433 (CCPA 1977).

Applicants have carefully considered the arguments, evidentiary support, and cited legal precedent set forth (in the Office Action) in support of the rejection under §103(a). With all due

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respect, the rejection relies on clearly erroneous statements of fact and legal precedent readily distinguishable in view of the facts of the present case.

The rejection cannot be maintained, first of all, because the cited references fail to meet all limitations on the rejected claims, which is necessary to demonstrate obviousness under §103(a). *Royka, supra*. As indicated above, the rejection relies on Siris to meet the claim limitation "treating lameness caused by osteoarthritis." The reliance is misplaced.

Siris does teach the use of a bisphosphonic acid derivative, as recited in the present claims, but not for the same use, i.e., method, as presently claimed. Siris teaches use of the bisphosphonic acid derivative in the treatment of Paget's disease, which neither teaches nor suggests treating lameness caused by osteoarthritis (as presently claimed), allegations to the contrary in the statement of rejection, notwithstanding. In fact, Siris neither teaches nor suggests, even, the treatment of osteoarthritis, let alone neither teaching nor suggesting the treatment of lameness caused by osteoarthritis, as required in the rejected claims.

It is true, as set forth in the statement of rejection, that osteoarthritis can be caused by Paget's disease (so called "secondary osteoarthritis"). Paget's disease causes bone deformity; which, in turn, can lead to osteoarthritis. Nevertheless, treating Paget's disease using a bisphosphonic acid derivative—as taught by Siris—if effective, neither teaches nor suggests "treating lameness caused by osteoarthritis," as presently claimed.

Paget's disease, according to Siris, would effectively prevent the bone deformity (caused by the disease) and, accordingly, prevent the secondary osteoarthritis (resulting from the bone

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deformity). In other words, at best Siris teaches preventing secondary osteoarthritis; which, of course, neither teaches nor suggests an effective treatment of pre-existing osteoarthritis.

The allegedly inherent teachings in Siris are not supported by the express teachings of the reference. To prevent occurrence of secondary osteoarthritis, it is best to prescribe antipagetic treatment to asymptomatic patients. This is apparent from the passage on page 340, third full paragraph of Siris "to prescribe antipagetic therapy to asymptomatic patients". In other words, Siris teaches: if a symptomatic pagetic patient with secondary osteoarthritis is treated with antipagetic treatment, this will merely stop progression of Paget's disease and further disease-effected bone deformation and resulting osteoarthritis; but it will not effectively reverse any pre-existing osteoarthritis.

Siris, of course, mentions nothing whatsoever about treating (or preventing) osteoarthritis-induced lameness. As such, the statement of rejection must rely on the theory of inherency, i.e., the statement of rejection alleges, in effect, that a person (or animal) suffering from osteoarthritis inherently suffers from lameness, as well. This finding is based on an erroneous understanding, and application, of controlling legal precedent.

Lameness does not, of course, necessarily afflict sufferers of osteoarthritis. And, in any event, the initial burden of evidence rests with the PTO to establish any allegedly inherent teachings in the prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPA & I 1990), which burden the PTO has failed to sustain. PTO "rejections on obviousness grounds cannot be sustained by mere conclusory

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statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

As explained in the foregoing paragraphs, Siris neither teaches nor suggests using a bisphosphonic acid derivative in treating either (1) osteoarthritis or (2) lameness caused by osteoarthritis; and, as such, Siris fails to meet the limitation "treating lameness caused by osteoarthritis" on the rejected claims, contrary to the allegations set forth in the statement of rejection. Since "the cited references do not support each limitation of [the rejected] claim[s]," the rejection under §103(a) is "inadequate on its face." *Thrift*, 63 USPQ2d at 2008.

Additionally, *Biere* cannot be used to support the rejection because it is not enabling with respect to the described treatment of osteoarthritis. Prior art relied on in a rejection under §103 must be *enabling*, i.e., "if the prior art of record fails to disclose or render obvious a method of making the claimed [invention] . . . it may not be legally concluded that the compound was in the possession of the public." *In re Hoeksema*, 158 USPQ 596, 601 (CCPA 1968).

[T]he description of the invention in the printed publication must be an "enabling" description. . . . Unless this condition prevails, the description in the printed publication is inadequate as a statutory bar to patentability.

In re Le Grice, 133 USPQ 365, 373-74 (CCPA 1962). To support enablement for an asserted therapeutic use requires test data and an explanation of why that data supports the asserted use. See, *Ex parte Maas*, 9 USPQ2d 1746 (Bd. Pat. App. & Inter. 1987); *Ex parte Balzarini*, 21 USPQ2d 1892 (Bd. Pat. App. & Inter. 1991).

According to *Biere* (column 1, lines 50-51)

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antiarthritic activity of the compounds of this invention forms the basis for therapy of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and other related diseases, especially of the collagen and the skeletal system (e.g., osteoporosis, Paget's disease, etc.).

Biere's asserted therapeutic use in the treatment of osteoarthritis must be taken as mere non-enabling speculation, i.e., the reference provides no test data, whatsoever, supporting the alleged "basis for therapy of . . . osteoarthritis." *Maas, supra. Balzarini, supra.* Since Biere is non-enabling with respect to the treatment of osteoarthritis, the reference fails to support the treatment of osteoarthritis—using any diphosphonic acid derivative—in the prior art. *Le Grice*, 133 USPQ at 373-74.

Biere's disclosure of "antiarthritic activity" is based on the disclosed diphosphonic acid derivatives having "anti-inflammatory activity." According to Biere (column 1, lines 39 and 42-43):

The compounds of this invention . . . possess a pronounced antiinflammatory and antiarthritic activity . . . in such a way that curative effects can clearly be proven to exist in rats with induced arthritis.

Biere further discloses (column 2, lines 20-24) that the arthritis induced in the rat animal model (by injection of a *Mycobacterium*) "resembles rheumatoid arthritis."

The teachings of Biere must be interpreted through the eyes of the skilled person in the art. *In re Hedges*, 228 USPQ 685 (Fed. Cir. 1985). The teachings of the reference—as viewed by one skilled in the art—must be reasonably predictive of the asserted therapeutic use. *Maas, supra.* Viewing Biere's disclosure of "anti-inflammatory and antiarthritic activity," the skilled artisan would find it reasonably predictive of efficacy in treating only inflammatory arthritic conditions such as rheumatoid arthritis. Nothing disclosed in Biere is reasonably predictive of successfully treating a

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non-inflammatory arthritic condition such as osteoarthritis. Applicant's evidentiary submissions and corresponding arguments, of record, regarding the teachings of Biere and the distinction of osteoarthritis/osteoarthritis from rheumatoid arthritis are equally relevant to the teachings of Biere. As demonstrated on the record—reference being made especially to the presentation made during the interview at the PTO on 6 June 2006 and to the evidence and accompanying remarks filed 6 October 2006 (with the RCE) in the PTO—one skilled in the art would have interpreted Biere's disclosure of anti-arthritic activity reasonably predictive only in connection with treatment of inflammatory arthritic conditions. In this respect applicants refer, in particularly,:

The evidence of record establishes that "osteoarthritis," as recited in the present claims, is unrelated to rheumatoid arthritis: rheumatoid arthritis is an inflammatory, autoimmune disease; whereas, osteoarthritis is a non-inflammatory, degenerative disease. The fact that both diseases affect the joints is merely consequential.

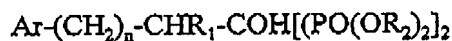
For the foregoing reasons, one skilled in the art would not have expected the treatments of Biere to be effective in "treating lameness caused by osteoarthritis"—as presently claimed—with a reasonable chance of success. Withdrawal of the rejection further appears to be in order.

The rejection also lacks the requisite motivation to combine references Biere and Barbier. Biere (column 1, lines 46-47) discloses aromatic bisphosphonic derivatives and their anti-inflammatory and antiarthritic properties. According to Biere (column 1, lines 53-57):

This antiarthritic activity of the compounds of this invention forms the basis for therapy of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and other related diseases, especially of the collagen and the skeletal system (e.g., osteoporosis, Paget's disease, etc.).

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Specifically, the disclosed aromatic derivatives have the general formula



wherein, variable "Ar is optionally substituted phenyl, naphthyl, biphenyl, or thienyl.

The statement of rejection admits (correctly) that the aromatic derivatives disclosed in Biere fail to meet the "bisphosphonic derivative" limitation on the present, rejected claims. Nevertheless, the rejection incorrectly alleges—in reference to the bisphosphonic acid derivatives disclosed in Barbier that meet those recited in the present claims—(as set forth above, emphasis added) "Biere et al. teaches that the antiarthritic [*sic*, antiarthritic] activity of the bisphosphonic acid derivatives is useful for the therapy of . . . osteoarthritis." Biere does not teach (or suggest) anything whatsoever concerning the bisphosphonic acid derivatives recited in the present claims that are disclosed in Barbier.

The rejection ignores the fact that the teachings of Biere—with respect to treating osteoarthritis—are limited to the aromatic derivatives disclosed in the reference, which disclosed derivatives neither teach nor suggest the bisphosphonic acid derivatives recited in the present claims.

It is impermissible within the framework of §103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.

Hedges, 228 USPQ at 687. The rejection also ignores the fact that the teachings of Barbier—with respect to the disclosed bisphosphonic acid derivatives meeting those recited in the present claims—are limited to their use in promoting bone repair, especially following a fracture or surgery. The aforesaid facts point to the necessity of explaining why the skilled artisan would have thought

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to "pick and choose" only the teachings of purpose/use from a first reference, and only the disclosure of compounds from a second reference directed to a different purpose/use than the first reference.

In other words, with all due respect the rejection fails to provide the requisite showing in the prior art of a motivation for one skilled in the art to have selected only certain bisphosphonic acid derivatives from among those disclosed in Barbier (i.e., those recited in the present claims) and used those selected derivatives for the use taught in Biere, in place of the different bisphosphonic acid derivatives that Biere uses. Finding two, isolated disclosures that can theoretically be combined in such a way as to meet the present claims does not render the combination obvious "unless the art also contains something to suggest the desirability of the proposed combination." *Bergel*, 130 USPQ at 208 (emphasis added).

The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.

Fritch, 23 USPQ2d at 1783-84 (emphasis added).

When prior art references require selective combination . . . [t]here must be "something in the prior art to suggest the desirability, and thus the obviousness, of making the combination" [*citation omitted*].

Interconnect Planning Corp., 227 USPQ at 551 (emphasis added). Why the skilled artisan would have desired to use the compounds of Barbier for the use/purpose of Biere, and where this desire can be found in the prior art, is not provided in the statement of rejection.

Note is taken that, as also correctly indicated in the statement of rejection (Office Action, page 6), Barbier (column 2, lines 44-49) (emphasis added) teaches:

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Several bisphosphonic acid derivatives are currently being developed on humans or marketed for use in the treatment of bone diseases such as Paget's disease and osteoporosis. These diseases are characterized by an osteoclastic stimulation (more significant in Paget's disease than in osteoporosis), which has to be checked.

Barbier does not more specifically identify the "Several" derivatives or, even, whether they are the same derivatives that Barbier uses.

Note is taken, further, that Siris (discussed above) teaches use of the bisphosphonic acid derivative recited in the present claims in treating Paget's disease. However, Siris does not teach or suggest whether these derivatives are, also, useful in promoting bone repair, the use according to Barbier.

Accordingly, the rejection fails to satisfy the requirement for demonstrating obviousness, under §103(a),

by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art *would lead* that individual to combine the relevant references. . . . Indeed, the teachings of the references can be combined only if there is some suggestion or incentive to do so.

Obukowicz, 27 USPQ2d at 1065 (*emphasis, added*). Withdrawal of the rejection further appears to be in order.

As indicated, above, the statement of rejection relies on *Atlas Powder Co.*, 61 USPQ2d at 1947, and *Best*, 195 USPQ at 433, to support the alleged standard of patentability

the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable [*emphasis added*].

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With all due respect, the alleged standard of patentability is erroneous and reliance on *Atlas Powder Co.* and *Best* is misplaced.

Contrary to the statement of rejection, the holding in *Best, supra* does not concern "claiming of a new use." At issue in *Best*, 195 USPQ at 431, were claims directed to a "crystalline zeolitic aluminosilicate" composition and process for making the claimed composition. Thus, *Best*, 195 USPQ at 433, held:

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product [emphasis added].

Accordingly, the holding in *Best* is limited to a "claimed product." Since use claims—such as "for treating lameness," as presently claimed—were not at issue in *Best*, any statements in the decision allegedly applicable to "the claiming of a new use" are mere *dicta* and, as such, the holding in *Best* does not, and cannot control in the present case. *Metropolitan Stevedore Co. v. Rambo*, 515 U.S. 291, 300 (1994) ("Breath spent repeating dicta does not infuse it with life"). The same applies to *Atlas Powder Co.*

Contrary to the position taken in the statement of rejection, as held in *Perricone v. Medicis Pharmaceutical Corp.*, 77 USPQ2d 1321, 1328 (Fed. Cir. 2005) (emphasis added):

New uses of old products or processes are indeed patentable subject matter. See 35 U.S.C. § 101 (2000) (identifying as patentable "any new and useful improvements" of a process, machine, manufacture, etc.); *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986) (principles of inherency do not prohibit a process patent for a new use of an old structure).

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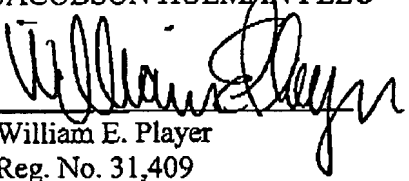
Under §103(a) the initial burden rests with the PTO to show that the presently claimed method—a new use of a known compound—is unpatentable. *Oetiker*, 24 USPQ 1444 and 1447. To satisfy this burden the PTO must show that "the [prior art] compound would be an effective [treatment for "lameness caused by osteoarthritis"] if administered in the dosage disclosed by [the prior art]." *In re Shetty*, 195 USPQ 753, 756 (CCPA 1977). The PTO has failed to satisfy this burden in the present case, i.e., since "none of the . . . compounds in any of the references . . . suggested a use, much less a dosage," for "treating lameness caused by osteoarthritis," it amounts to "mere hindsight . . . untenable for establishing obviousness." *Shetty*, 195 USPQ at 756-77. Accordingly, withdrawal of the rejection under §103(a), further, appears to be in order.

Favorable action is requested.

Respectfully submitted,

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